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When do patients given intrathecal morphine need postoperative systemic opiates?

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Summary

A prospective, randomised study has compared the requirements for intramuscular papaveretum after cholecystectomy in patients given either 0.8 mg intrathecal morphine preoperatively or intravenous papaveretum peroperatively.

Patients given intrathecal morphine required significantly less papaveretum during the first 48 hours after operation, but no significant difference in analgesic requirements was observed by 72 hours due to a continuing demand for papaveretum by these patients.

Introduction

Morphine injected into the cerebrospinal fluid of animals binds to opiate receptors in the neuroaxis to produce intense and prolonged analgesia *(1)*. The initial enthusiasm with which this laboratory finding was applied to the problems of postoperative pain control has been tempered by criticism of anecdotal reports and uncontrolled trials which failed to compare intrathecal morphine with conventional methods of achieving postoperative analgesia *(2,3)* and by reports of side-effects, in particular respiratory depression, occurring in patients given intrathecal opiates *(4)*.

This randomised, prospective study was designed to compare the requirements for a postoperative systemic opiate in patients receiving either preoperative intrathecal morphine or peroperative intravenous papaveretum.

Patients and methods

Female patients undergoing elective cholecystectomy gave their informed consent for inclusion in the study and were randomised into two groups having received 10 mg of oral diazepam as premedication. Group A (10 patients) received 0.8 mg preservative-free morphine in a volume of 4 ml injected intrathecally through the L 2–3 interspace using a 25 gauge spinal needle 15 minutes before induction of anaesthesia: peroperative analgesics were not given. Group B (10 patients) received intravenous papaveretum intermittently during the operation. All patients were anaesthetised using althesin, nitrous oxide and alcuronium; all operations consisted of a subcostal, muscle-cutting incision, cholecystectomy, cholangiography and insertion of a subhepatic drainage tube. Patients who underwent exploration of the common bile duct were excuded from the study.

Patients were studied for 72 hours after operation and were nursed during the first 24 hours in a high-dependency unit where respiratory rate, blood pressure and pulse rate were recorded hourly. Patients were asked every hour if they were in pain, but sleeping patients were not disturbed. Nurses in attendance were allowed to administer a single I.M. injection (5 mg) of papaveretum to patients in Group A, but were instructed to call the anaesthetist if additional injections were needed: patients in Group B were prescribed I.M. papaveretum (10, 15 or 20 mg) 3 or 4 hourly. Patients in each group were treated identically after 24 hours and were nursed on a general surgical ward. Intramuscular papaveretum was given as doses of 10, 15 or 20 mg according to the nurse's assessment of the degree of pain experienced by each patient, although not all patients complaining of pain or discomfort were given papaveretum. Respiratory rate, blood pressure and pulse rate were recorded every four hours for a further 24 hours.

Results were analysed by the Wilcoxon rank sum test for unpaired data. Statistical significance was assumed when $P<0.05$. The study was approved by the Hospital Ethical Committee.

Results

Age, weight and preoperative blood pressure and pulse rate did not differ significantly between the two groups (Table I).

TABLE I *Patient details (mean ± s.d.)*

	Group A	*Group B*
Age (yr)	47.5 ± 5.4	42.7 ± 15.5
Range	37–54	24–65
Weight (kg)	64.5 ± 10.5	64.5 ± 13.8
Range	41–80	50–88
Preoperative blood pressure (mmHg)		
systolic	120 ± 15	128 ± 12
diastolic	80 ± 10	80 ± 7
Preoperative pulse rate (per min)	79 ± 9.1	81 ± 12.5

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The mean ± s.d. dose of pavaveretum given peroperatively to patients in Group B was 16.8 ± 2.3 mg.

CLINICAL PARAMETERS (Fig. 1)

Patients in Group A maintained a significantly lower systolic blood pressure than patients in Group B during the first 24 hours but the only significant difference in mean pulse rate between the two groups was recorded 20, 28 and 32 hours postoperatively. No significant difference in respiratory rates was found and no patient developed respiratory depression.

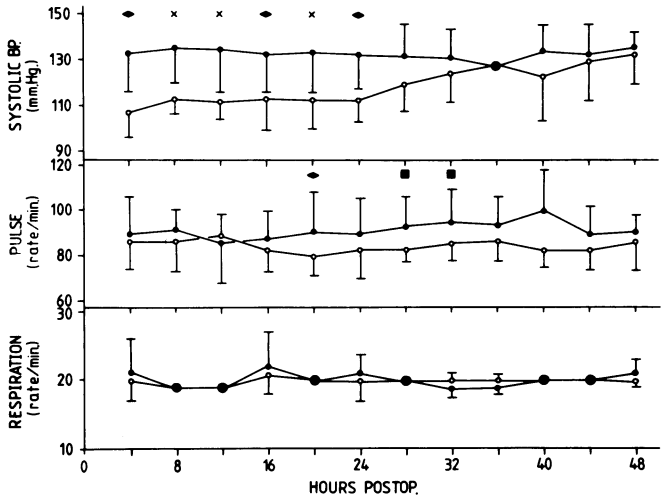

FIG. 1 Systolic blood pressure, pulse rate and respiratory rate in patients receiving preoperative intrathecal morphine open circles—Group A) or postoperative I.M. papaveretum (closed circles—Group B). ((x = $P<0.002$: ◆$P<0.02$: ■$P<0.05$).

PAIN CONTROL (Table II)

All patients in Group B complained of pain within the first 6 hours of operation compared to only 4 patients in Group A; the number of patients who complained during the subsequent 18 hours was consistently higher in Group B than in Group A, although this difference was least marked between 19 and 24 hours postoperatively.

TABLE II *Postoperative pain control: the number of patients complaining of pain during the first 24 hours after operation*

Time after operation (hours)	*Group A (Intrathecal morphine) n = 10*	*Group B (Control) n = 10*
0–6	4	10
7–12	2	8
13–18	2	5
19–24	5	7
0–24	6	10

ANALGESIC REQUIREMENTS (Fig. 2: Table III)

Four patients in Group A received papaveretum (mean dose ± s.d. 8 ± 11.1 mg/patient) during the first 24 hours compared to 10 patients (mean dose ± s.d. 50 ± 16.2 mg/patient) in Group B ($P<0.001$). However there was no significant difference in the dosage of papaveretum given to patients in each group between 24 and 48 hours postoperatively (Group A: 27 ± 4.9 mg/patient vs Group B: 19 ± 12.6 mg/patient). The total dosage of papaveretum given to patients in each group was significantly greater in Group B during the first 48 hours postoperatively, but statistical significance was not achieved when comparisons were made at 72 hours postoperatively due to a continuing requirement for papaveretum by patients in Group A.

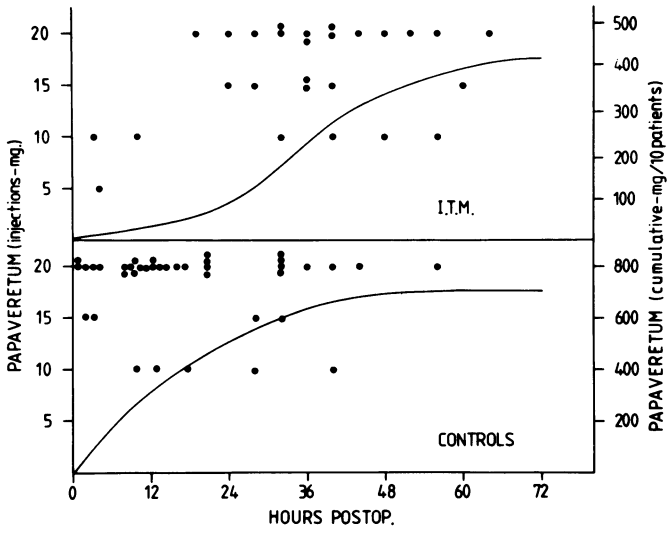

FIG. 2 Doses of papaveretum given postoperatively to patients receiving intrathecal morphine (ITM—Group A) and those acting as controls (Group B). Intramuscular injections are shown as single points; each curve represents the cumulative dosage of papaveretum given to each group.

TABLE III *Postoperative analgesic requirements*

Time interval after operation (hours)	*Mean ± s.d. Dosage papaveretum (mg/patient)* *Group A Intrathecal morphine*	*Group B Control*	*P*
0–24	8 ± 11.1	50 ± 16.2	<0.01
0–48	35 ± 27.9	69 ± 25.8	<0.05
0–72	43.5 ± 34.6	71 ± 27.1	NS

Discussion

The first clinical use of intrathecal morphine demonstrated profound analgesia in patients with malignant disease *(6)*. Since then it has been used most frequently to prevent postoperative pain in adults *(4,7)* and children *(8)* but its widespread use has been curtailed by complications, the most serious being respiratory despression which may have a delayed onset *(4,5)*. This complication is related to the dose of morphine used but its incidence is difficult to ascertain. No case of respiratory depression requiring naloxone was recorded in one series of 30 patients given 0.02 mg kg^{-1} intrathecal morphine *(7)*, whereas Jones *et al.* (1984) reported an incidence of 10.4% in a group of 29 children receiving the same dosage. A nationwide survey of anaesthetists in Sweden *(5)* reported an incidence between 4 and 7% in patients receiving beteeen 0.8 and 2.0 mg. Hence, any patient given intrathecal morphine preoperatively should be nursed on an intensive care or high dependency unit for 24 hours after operation and the additional use of systemic opiates restricted.

We took these precautions. The use of intrathecal morphine (0.8 mg) that was chosen seemed likely to be both effective and, as we have demonstrated in this limited study, free of the risk of respiratory depression. Unfortunately, pain control using this dosage was not ideal. Six patients experienced pain within 24 hours of operation, four of whom were given papaveretum. Similarly, Jones *et al. (8)* found that 34% of children given either 0.02 or 0.03 mg kg^{-1} intrathecal morphine required papaveretum within 24 hours of operation.

Postoperative pain is difficult to quantify but an indirect assessment can be made by monitoring the doses of a drug needed to achieve adequate analgesia. As expected, the

majority of papaveretum injections were given to patients in both groups within the first 48 hours postoperatively. Control patients required significantly more papaveretum during the first 24 hours than patients given intrathecal morphine. However, patients given intrathecal morphine required an unexpectedly high dosage of papaveretum between 24 and 48 hours, contrasting the dramatic reduction in dosage given to control patients during this period. A possible explanation for this observation is that patients did not expect to suffer increasing levels of pain when the analgesia produced by intrathecal morphine began to wane.

We have shown that 0.8 mg intrathecal morphine reduced the postoperative requirement for a systemically administered opiate when compared to a control group of patients and that this reduction was statistically significant during the first 48 hours postoperatively. The continued requirement for papaveretum beyond 48 hours by patients given intrathecal morphine negated statistical significance by 72 hours. The findings of this study, when considered alongside the established risk of respiratory depression when intrathecal morphine is used in large doses, suggests that this method of achieving postoperative analagesia should only be used when its advantage to the patient can be guaranteed by diligent postoperative observation and care.

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Notes on Books

A Colour Atlas of Haemorrhoid Management by R E B Taggart. 71 pages, illustrated. Wolfe Medical, London. £10.00.

This short book contains 40 full page colour photographs of good quality, many being taken through a proctoscope. The anatomy, pathology, diagnosis and management of haemorrhoids are described and a short section devoted to differential diagnosis. The author points out that every experienced proctologists has a preferrred pattern of management of haemorrhoids and this atlas is intended to give a starting point to those relatively inexperienced.

Optoelectronics in Medicine edited by Wilhelm Waidelich. 273 pages, illustrated, paperback. Springer, Berlin. $29.10.

This book contains the Proceedings of a Congress held in 1983 on the use of lasers in medicine. It includes contributions on the use of lasers in cancer surgery, neurosurgery, general surgery, gastroenterology, urology, gynaecology and dermatology. The contents provide a survey of the possibilities and limits of the utilisation of lasers in these fields. Many of the papers are in the German language which may limit their usefulness to British readers.

Orthopaedic Diagnosis by Hubert A Sissons, Ronald O Murray and H B S Kemp. 403 pages, illustrated. Springer, Berlin. £56.00.

This book consists of 94 problems of orthopaedic diagnosis and covers clinical, radiological and pathological aspects of bone disease. It is extensively illustrated with over 500 figures, many in colour, of radiographs and histological appearances. Selective references are given.

An original presentation which makes good reading for all with an interest in bone disorders.

Tutorials in Surgery 5: Surgical Pathology II by F G Smiddy and P N Cowen. 273 pages, illustrated. Pitman, London. £14.50.

This book is written jointly by a surgeon and pathologist and deals with the application of pathology to surgical practice. It is intended to give surgeons an understanding of the basic pathology of those diseases which present for surgical treatment. The volume covers blood disorders, the lymphatic system, breast, nervous system, respiratory system, heart disease, urinary tract, female genital tract and diseases of bones, joints and muscles.

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